

## Development of analgesic peptide therapeutics for AIDS-related neuropathic pain

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Chronic neuropathic pain is a huge problem to the health and well-being of an increasingly ageing population in the US, as substantiated by the large unmet clinical need associated with this type of pain, with estimates of 30-50% of sufferers refractory to existing medication. Thus, there is an imperative to increase knowledge of mechanisms of action of the key proteins in nociceptive pathways *in vitro* and to extend this knowledge to *in vivo* models of neuropathy to advance therapeutic development in this area. N-type voltage-gated  $\text{Ca}^{2+}$  channels (CaV2.2) have emerged as potential novel targets for the treatment of chronic neuropathic pain. Funded, in part, by a FORCES grant, we have identified two novel derivatives of the parent 15 amino acid CBD3 peptide, derived from collapsin response mediator protein 2 (CRMP-2) that suppressed inflammatory and neuropathic hypersensitivity by inhibiting CRMP-2 binding to N-type voltage gated calcium channels (CaV2.2) [Brittain *et al.*, *Nature Medicine* 17:822-829 (2011)]. Pharmacokinetic studies revealed nanogram levels of peptide in plasma of rats systemic administration consistent with relief of hypersensitivity. Furthermore, we observed improved and broader efficacy of the derivatized peptides in AIDS-therapy and nerve-injury related neuropathic pain models. Future studies regarding dosing and route of delivery optimization as well as identification of peptide-mimetics are ongoing to fully realize the commercial value of the peptides. Supported by the Startup program at the Indiana University Research & Technology Corporation (IURTC), we have setup Sophia Therapeutics LLC and together with IURTC are committed to the work proposed here.